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| EXAMINER LEAVITT, MARIA GOMEZ | | | | |
| ART UNIT 1633 | | PAPER NUMBER | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary

Application No.

10/573,813

Applicant(s)

WADA ET AL.

Examiner

MARIA LEAVITT

Art Unit

1633

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20, 22-26 and 29-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-20, 22-26 and 29-40 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

- I. Claims 1-3 and 38-40 drawn to a **method for producing lactic acid**, which comprises culturing hetero-lactic acid fermentation bacteria, wherein activity of pyruvate formate-lyase (**pfl**) **is inactivated** or decreased.
- II. Claims 4-6 and 35-37 drawn to a **method for producing lactic acid**, which comprises culturing bacteria, wherein activity of *Escherichia coli*-derived NADH-dependent D-lactate dehydrogenase (**IdhA**) **is enhanced** and activity of **pfl is inactivated** or decreased.
- III. Claims 7-9 drawn to a **microorganism** in which activity of FAD-dependent D-lactate dehydrogenase (**dld**) inherent in the microorganism is inactivated or decreased, activity of pfl is inactivated or decreased, and/or activity of *Escherichia coli*-derived NADH-dependent ldhA is enhanced.
- IV. Claims 10, 11 and 32-34 drawn to a **method for producing D-lactic** comprising culturing a microorganism in which activity of dld inherent in the microorganism is inactivated, activity of pfl is inactivated, and/or activity of *Escherichia coli*-derived NADH-dependent ldhA is enhanced.
- V. Claims 12-14 and 29-31 drawn to a **method for producing D-lactic** comprising culturing a microorganism in which activity of dld is inactivated or decreased.

- VI. Claims 15-17 drawn to **a microorganism** in which the gene encoding *Escherichia coli*-derived NADH-dependent IdhA expresses the NADH-dependent IdhA on the genome of the microorganism by using a promoter of a gene which controls expression of a protein involved in a glycolytic pathway, a nucleic acid biosynthesis pathway or an amino acid biosynthesis pathway.
- VII. Claims 18-20 drawn to **an *E. coli*** in which the gene encoding *Escherichia coli*-derived NADH-dependent IdhA expresses the NADH-dependent IdhA on the genome of the microorganism by using a promoter of a gene which controls expression of a protein involved in a glycolytic pathway, a nucleic acid biosynthesis pathway or an amino acid biosynthesis pathway.
- VIII. Claims 22-26 drawn to **a microorganism** having a TCA cycle, wherein activity of malate dehydrogenase (mdh) is inactivated, activity of pfl is inactivated, and/or activity of FAD-dependent dld is inactivated.

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical reasons:

37 CFR 1.475 (c) states:

"If an application contains to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present"

37 CFR 1.475 (d) also states:

"If multiple products, processes of manufacture, or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention

of each of the other categories related thereto will be considered as the main invention in the claims, see PCT article 17(3)(a) and 1.476(c)".

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical reasons: the technical feature linking groups I-VIII appears to be that they all relate to methods and products for producing lactic acid in a fermentation process by culturing a microorganism wherein the activity of the NADH-dependent D-lactate dehydrogenase (IdhA) may be enhanced and the activity of the pyruvate formate-lyase (pfl) may be inactivated or decreased. However, mutants of *E. coli* having elevated IdhA activity (Yang et al., *Metab. Eng.* 1999, pp. 141-52) or defective in pfl activity (Zhou et al., *Applied and Environmental Microbiology*, pp. 399-407; Yang et al., *Metab. Eng.* 1999, pp. 141-52) were already known in the art, at the time the invention was made. Therefore, the technical feature linking the invention of groups I-VIII does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over prior art for the reasons set forth above.

The inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Inventions of Groups I-VIII are drawn to materially different and distinct inventive concepts, having different chemical structures, physical properties and biological functions. For example, inventions of Group I is drawn to a method of producing lactic acid comprising culturing a mutant bacterium wherein the activity of the pfl is inactivated which is structurally

and functionally different from inventions of Group II drawn to a method of producing lactic acid comprising a mutant bacterium wherein the activity of the pfl is inactivated and the activity of the IdhA is enhanced. In addition, inventions of Groups V are drawn to a method for producing D-lactic comprising culturing a microorganism in which activity of FAD-dependent D-lactate dehydrogenase (dld) is inactivated which is structurally and functionally different from inventions of Groups I or II. Inventions of Groups III, VI, VII and VIII are drawn to microorganisms (e.g., *Sporolactobacillu*, *Lactbacillus delbrueckii*) or *E. coli* having different chemical structures, physical properties and biological functions because of attenuating or enhancing metabolic enzymatic activities. For example, dld inherent in the microorganism is inactivated, pfl is inactivated, and/or *Escherichia coli*-derived NADH-dependent ldhA is enhanced in the microorganism of Group III, *Escherichia coli*-derived NADH-dependent IdhA expresses the NADH-dependent IdhA on the genome of the microorganism, e.g., *Sporolactobacillu*, *Lactbacillus delbrueckii* in the microorganism of Group VI, the gene encoding *Escherichia coli*-derived NADH-dependent IdhA expresses the NADH-dependent IdhA on the genome of the microorganism by using a promoter of a gene controlling the expression of a gene that participates in a glycolytic pathway, a nucleic acid biosynthesis pathway or an amino acid biosynthesis pathway in an *E. coli* of Group VII activity of malate dehydrogenase (mdh) is inactivated, activity of pfl is inactivated, and/or activity of FAD-dependent dld is inactivated in microorganism of Group VIII.

The claims in Groups I-VIII are drawn to distinct products and methods that utilize distinct steps, requiring non-coextensive search and examination. Thus, it follows from the preceding analysis that the claimed inventions listed as Groups I-VIII do not relate to a single

inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding technical features for the reasons set forth above.

MPEP 1893.03(d) states:

If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined. See MPEP § 821.04 and § 821.04(a). Any nonelected processes of making and/or using an allowable product should be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

Species restriction

Should Group III be elected, a species restriction is further required under 35 U.S.C. 121 and 372, wherein a species election(s) must correspond to an elected group as indicated above. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

- 1) a) dld activity inherent in the microorganism is inactivated, activity of pyruvate formate-lyase (pfl) is inactivated or decreased and activity of *Escherichia coli*-derived NADH-dependent D-lactate dehydrogenase (ldhA) is enhanced;
- b) dld activity inherent in the microorganism is inactivated;
- c) activity of pyruvate formate-lyase (pfl) is inactivated or decreased and
- d) activity of *Escherichia coli*-derived NADH-dependent D-lactate dehydrogenase (ldhA) is enhanced, as recited in claim 7.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special

technical features for the following reasons: the species are drawn to metabolically engineered **microorganisms** having different chemical structures, physical properties, and biological functions as the results of having different genes disrupted or enhanced. As the technical feature of a gene coding for an enzyme, linking the members do not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature, the requirement for unity of invention is not fulfilled.

Applicant is required, in reply to this action, to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 1, 4, 7, 10, 12, 15 and 22 are generic.

Should Group **VI** be elected, a species restriction is further required under 35 U.S.C. 121 and 372, wherein a species election(s) must correspond to an elected group as indicated above. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

- 2) a) pyruvate formate-lyase (pfl) inherent in the microorganism is inactivated and activity of FAD-dependent D-lactate dehydrogenase (dld) is inactivated;
- b) pyruvate formate-lyase (pfl) inherent in the microorganism is inactivated; and
- c) activity of FAD-dependent D-lactate dehydrogenase (dld) is inactivated, as recited in claim 17.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the species are drawn to metabolically engineered **microorganisms** having different chemical structures, physical properties, and biological

functions as the results of having different genes disrupted or enhanced. As the technical feature of a gene coding for an enzyme, linking the members do not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature, the requirement for unity of invention is not fulfilled.

Applicant is required, in reply to this action, to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 1, 4, 7, 10, 12, 15 and 22 are generic.

Should Group **VIII** be elected, a species restriction is further required under 35 U.S.C. 121 and 372, wherein a species election(s) must correspond to an elected group as indicated above. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

3) a) malate dehydrogenase (mdh) is inactivated and activity of FAD-dependent D-lactate dehydrogenase (dld) is inactivated

b) malate dehydrogenase (mdh) is inactivated, and

c) activity of FAD-dependent D-lactate dehydrogenase (dld) is inactivated, as recited in claim 22.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the species are drawn metabolically engineered **microorganisms** having different chemical structures, physical properties, and biological functions as the results of having different genes disrupted or enhanced. As the technical feature of a gene coding for an enzyme, linking the members do not constitute a special technical feature

as defined by PCT Rule 13.2, particularly since each of the species does not share a substantially common structural feature, the requirement for unity of invention is not fulfilled.

Applicant is required, in reply to this action, to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, at least claims 1, 4, 7, 10, 12, 15 and 22 are generic.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) and identification of the claims encompassing the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Art Unit: 1633

/Maria Leavitt/

Maria Leavitt, Ph.D.
Examiner, Art Unit 1633